Hypoparathyroidism

Medical and Surgical Aspects

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• **Hypoparathyroidism is almost invariably a complication of operation on the thyroid gland, and the diagnosis usually presents no problem. Fairly good control of the symptoms is possible by medical management, but, since substitution therapy is not available, the treatment of hypoparathyroidism is not completely satisfactory. Parathyroid homografting has been attempted; at present, however, grafting procedures must be considered experimental.**

HYPOPARATHYROIDISM is essentially a complication of surgical operation on the thyroid gland. Buchwalter[5] reported a 3 per cent incidence of permanent parathyroid deficiency in a series of 600 thyroid operations at a university hospital. The incidence of this complication in any series probably depends largely upon the proportion of operations performed for carcinoma of the thyroid. Less important causes of parathyroid tetany are congenital absence of the parathyroid glands, idiopathic hypoparathyroidism and a transient stage following the removal of a parathyroid adenoma.

The subtotal removal of parathyroid tissue during the course of thyroidectomy may lead to symptoms of hypoparathyroidism of a few days' to a few weeks' duration which readily respond to antitetany therapy. It is the plight of patients after inadvertent extirpation of all the parathyroid glands that is the concern of this paper. They may be reduced to pathetic states if available therapy is ineffective.

The crucial factor is the elimination of the parathyroid hormone, with the resultant changes in calcium and phosphorus metabolism. The production of ionized calcium, which plays an important role in regulating neuromuscular irritability, is dependent upon the integrity of the parathyroid glands and adequate absorption of calcium from the gastrointestinal tract. The parathyroid hormone maintains constant serum calcium and phosphorus levels by governing the renal threshold for phosphates. Hypoparathyroid tetany, due to an elevation of serum phosphate and a lowering of serum calcium, leads to body alterations involving the nervous system and epithelial structures.

The milder forms of postoperative tetany due to partial removal of the parathyroid glands, results in insidious complaints secondary to increased neuromuscular irritability. The tetany following complete removal of the parathyroids, however, is characteristically explosive in onset: Shortly after operation on the thyroid gland—usually within 24 hours—the patient becomes apprehensive and complains of tingling of the fingers and toes. Carpopedal spasm quickly follows, and if treatment is not begun, the patient may die of generalized convulsions and laryngospasm.

After the patient is nursed through the acute state, chronic tetany remains. Primarily neuromuscular in origin, the symptoms include weakness, lethargy and somnolence. Moreover, during periods of stress all the symptoms of acute tetany may reappear. Sometimes, psychosis develops; rarely roentgenological examination reveals calcification of the basal ganglia of the brain.[4] In cases of long standing, changes in the epithelial structures occur. Transverse ridging of the finger and toenails and a susceptibility to fungus infections of the skin and mucous membranes are of periodic annoyance. A more serious complication is the formation of presenile cataracts.[4,5]

Interestingly, partial relief of the symptoms of hypoparathyroidism may occur with the onset of pregnancy,[3] the fetal parathyroid glands apparently being capable of sustaining the mother to some degree.

The diagnosis of parathyroid tetany presents no problem unless the characteristic onset is delayed. Theoretically this occurs when most of the parathyroid tissue is surgically removed and the blood supply to the remainder is damaged. Thrombosis of the vessels and necrosis of the residual parathyroid tissue may result in late symptoms of hypocalcemic tetany. More often, suspicion is aroused by the typical sequence of events following operation on the thyroid gland. Latent tetany can be demonstrated by a twitching of the facial muscles when the facial nerve anterior to the ear is tapped (Chvostek's sign), or by eliciting carpal spasm on applying a tourniquet to the forearm (Trousseau's sign).

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Increased excitability of these muscles may also be demonstrated by galvanic stimulation (Erb's sign).

Laboratory tests then can be used to confirm the diagnosis. Hypoparathyroid tetany is associated with a decrease in serum calcium (normal 9 to 11 mg. per 100 cc.) and an increase in serum phosphorus (normal 2.5 to 4 mg. per 100 cc.). Urinary excretion of calcium, as demonstrated by the Sulkowitch test, decreases. More sophisticated studies of parathyroid malfunction are usually unnecessary.

TREATMENT

The treatment of hypoparathyroidism may be lifesaving if acute symptoms of tetany develop immediately following thyroid operations. The replacement of serum calcium is paramount. This is most rapidly done by injecting 10 cc. of 10 per cent calcium gluconate intravenously. The patient can then be maintained by slow intravenous drip of 10 cc. of 10 per cent calcium chloride diluted in 500 cc. of normal saline solution. Calcium chloride is too irritating to be used undiluted and will result in a serious slough if injected subcutaneously. Parathormone is used infrequently in acute tetany. Sometimes emergency tracheostomy is necessary to relieve laryngospasm unresponsive to intravenous calcium therapy.

If all the parathyroid glands have been excised, intravenous infusion of calcium cannot be discontinued until the treatment for chronic tetany is instituted. The chronic form of hypoparathyroid tetany requires treatment for an indefinite period. Prolonged therapy falls into five categories: (1) Use of drugs that increase the absorption of calcium from the gastrointestinal tract; (2) use of drugs that act on the kidney tubules, decreasing phosphate reabsorption and thus increasing the excretion of this cation in the urine; (3) adding absorbable calcium salts to the diet; (4) avoidance of calcium-binding foods, and (5) ingestion of phosphate-binding foods.

1. Vitamin D (Calciferol®), 50,000 to 200.000 units per day, is the drug of choice for increasing calcium absorption from the gastrointestinal tract. Dihydrotachysterol (AT 10, Hytakerol®) is equally effective but more expensive—one capsule (0.625 mg.) per day is the usual dose.

2. AT 10 also serves to maintain a normal serum calcium level by decreasing phosphate reabsorption by the renal tubules. Similar action on the kidney by parathormone is of less importance, since the rapid development of tolerance renders this drug valueless in clinical practice.

3. Supplemental calcium is often administered orally in the form of calcium lactate or calcium gluconate (5 to 10 gm. per day). Although containing a higher concentration of calcium, calcium chloride cannot be used in most cases because of intolerance by the gastrointestinal tract.

4. Calcium-binding foods are avoided within dietary reason. Phosphates (dairy products), and oxalates (spinach, rhubarb, chocolate) are the chief offenders.

5. Phosphate-binding drugs (Amphojel,® Gelusil®) can be used to advantage to decrease absorption from the gastrointestinal tract and thereby lower the serum phosphate level.

The surgical treatment of hypoparathyroidism starts at the operating table during operation on the thyroid gland. If parathyroid tissue can be identified in the removed specimen, the glands are immediately transplanted into the neck muscles. (Experimentally, a definite percentage of these autografts survive.[12,18]) Clinically, the value of this procedure is open to conjecture since the surgeon never is certain whether it is the graft or perhaps residual parathyroid tissue that is maintaining the patient's calcium balance. Moreover, the inadvertent removal of one or more parathyroid glands is usually not discovered until several days later when the pathologist is making a microscopic study of the specimen.

Ideally, homotransplantation of parathyroid glands is the answer to the problem of hypoparathyroid tetany. Until recently, attempts at homografting were uniformly unsuccessful[10,13] owing to immune response by the host (reportedly successful results were poorly documented). There is, of course, no genetic incompatibility when the donor and recipient are identical twins.

Among the methods attempted to delay or circumvent the immune reaction are the use of embryonic tissue for donor material,[14,19,22] ensheathing the graft in a millipore filter,[1] tissue culture techniques of delayed transplantation[8] and radiation of the host to weaken the immune response by destroying the capacity for antibody formation.[9] Perhaps the most promising method of parathyroid transplantation takes into account the theoretical decreased antigenicity of fetal tissue and the increased chances of success of vascularized grafts.[12] Sterling[20,21] reported three successful transplants with this method, using as donors full term infants that died soon after birth. Unfortunately, no other surgeon has been able to duplicate these results although apparently some of them have improved upon the operative technique.[2,6,7,11,17] In another recent case, in which a successful result was reported with the use of a vascularized fetal graft,[23] the transplant is now known to be a failure.[16]

I have transplanted a vascularized parathyroid graft, from a two-pound fetus that did not survive premature birth at six months, to a 12-year-old

child. The operation was done under ideal circumstances, and the anastomosis of vessels to the host was completed within two and a half hours of the death of the premature infant. Despite an immediate "take" of the graft, as demonstrated by reexploration of the wound one week later, and early dramatic clinical improvement of the patient, the long-term result has been disappointing.

As Murray[15] pointed out, convincing proof of a successful parathyroid homograft has not been established, and it becomes increasingly apparent that a favorable outcome in this field awaits the solution to the general problem of the antigenic rejection of homografts. At present, homotransplantation of parathyroid tissue must be considered experimental.

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